HOAU-YAN WANG, Ph.D.

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EDUCATION:

Medical College of PA, Philadelphia, PA	1988 - Pharmacology, Ph.D.
St. John's University, New York, NY	1985 - Pharmacology, M.S.
China Medical College, Taiwan	1981 - Pharmacy, B.S.

EMPLOYMENT:

2019-present	CUNY School of Medicine at City College, New York, NY Medical Professor, Molecular, Cellular & Biomedical Sciences
2001-2019	CUNY Medical School at City College, New York, NY Associate Medical Professor, Physiology, Pharmacology & Neuroscience **(Tenured, May 2006)**
2001	R.W. Johnson Pharmaceutical Research Institute, Spring House, PA Principal Scientist, CNS Research
1998 - 2000	R.W. Johnson Pharmaceutical Research Institute, Spring House, PA Senior Scientist, CNS Research
1998 - 2001	MCP-Hahnemann University School of Medicine, Philadelphia, PA Adjunct Assistant Professor, Pharmacology & Physiology
1994 - 1997	Allegheny University of the Health Sciences/MCP, Philadelphia, PA Assistant Professor, Pharmacology & Psychiatry
1992 - 1994	Medical College of PA (MCP), Philadelphia, PA Assistant Professor, Psychiatry
1990 - 1992	Medical College of PA (MCP), Philadelphia, PA Instructor, Psychiatry

CURRENT RESEARCH INTERESTS:

- Age-dependent alterations in neuronal function and the underlying mechanisms.
- Pathogenic mechanisms and therapeutic targets for neurodegeneration in Alzheimer's disease

- Pathogenic mechanisms and therapeutic targets for neuropsychiatric disorders with particular emphasis on bipolar affective disorder and schizophrenia.
- Discovery of novel therapeutic agents and diagnostic biomarkers for neurodegenerative and psychiatric disorders as well as traumatic brain injury.
- Molecular pharmacology, target identification and therapeutic mechanism of psychoactive drugs.

LABORATORY TECHNIQUES AND RESEARCH EXPERTISE:

1. Protein biochemistry, physiology and pharmacology of ionotropic and metabotropic receptors as well as trophic factor receptors.

- Receptor/G protein interactions including GTP binding, calcium signaling, identification and characterization of signal transduction pathways, second messenger (Ca^{2+}, cAMP, cGMP & phosphoinositide) measurement, Lipid acylation, Toxin-activated ADP-ribosylation, lipid peroxidation & reactive oxygen species assessment.
- Protein purification and characterization, immunoprecipitation, 1-D/2-D gel electrophoresis, Western blotting, protein phosphorylation/dephosphorylation, protein kinase and enzymatic activity assay, antibody purification & characterization.
- Receptor binding assay, RIA, EIA, high throughput screening, receptor autoradiography.

2. Molecular and Cellular biology

- General molecular biology techniques-Northern and Southern blotting, cDNA library screening.
- General recombinant DNA techniques (cloning to recombinant protein expression).
- Cell culture, cell proliferation & differentiation, cell death assay.

3. Bioinformatics

- Sequence database mining using bioinformatic software tools. Experience with Incyte blast tools, and Incyte databases, NCBI databases.
- Proteomics technology and protein sequencing.

CONTRIBUTION TO SCIENCE

1. My early publications elucidated the molecular mechanism responsible for lithium's pharmacological actions relevant to its efficacy in treating bipolar disorder. My data from several functional studies were the first to show that lithium has a profound inhibitory effect on protein kinase C (PKC) activation at therapeutic doses. Based on this finding, I hypothesized that PKC is overly activated in CNS and peripheral tissues from bipolar patients and that this over-activation could be used as a biomarker to support the diagnosis of this disorder. This hypothesis was proven correct by the findings that membrane-associated PKC is substantially higher in postmortem brain tissues and blood platelets of bipolar subjects in their manic and euthymic states. Lithium and valproate treatments attenuate such hyperactivated PKC by reducing its Ca^{2+}-dependent cytosol to membrane translocation, the primary activation mechanism for PKC. By providing molecular underpinning and a peripheral state-dependent biomarker for bipolar disorder, this body of work has paved the way to improve the therapeutic efficacy for bipolar disorder treatments. More importantly, this biomarker provides a method of monitoring this disease and therapeutic effects aiming to stabilize bipolar disorder. I served as the primary investigator or co-investigator in all of these studies.

a. Wang HY, Friedman E (1989) Lithium inhibition of PKC activation and activation-induced serotonin release. Psychopharmacol 99: 213-218.
b. Friedman E, Wang HY, Levinson D, Connell TA, Singh H (1993) Altered platelet protein kinase C activity in bipolar affective disorder, manic episode. Biol Psychiatry 33:520-525.

c. Wang HY, Friedman E (1996) Enhanced protein kinase C activity and translocation in bipolar affective disorder brain. Biol Psychiatry 40:568-575.
d. Wang HY, Markwitz P, Levinson D, Undie AS, Friedman E (1999) Increased membrane-associated protein kinase C activity and translocation in blood platelets from bipolar affective disorder patients. J Psychiatric Res 33: 171-179.

2. I investigated the molecular mechanism underlying the long-lasting detrimental effects on cognitive function in offspring of cocaine abuse during pregnancy. My initial efforts led to a discovery that, in contrast to common belief, prenatal cocaine exposure affects specific targets such as D_1 dopamine receptors, leading to distorted dendrites and behavioral dysfunction. More importantly, I observed a substantial increase in membrane-associated protein kinase C (PKC) – similar to that in bipolar disorder – in key brain regions that lasted well into adulthood. Based on this finding and the fact that glutamatergic systems are intimately related to cognitive function, I hypothesized that hyperactivated PKC is the molecular culprit responsible for glutamatergic and hence cognitive dysfunction. This hypothesis was supported by our findings that protracted membrane association of specific PKC isoforms is at least in part responsible for defective AMPA receptor and mGluR1 function. By elucidating the molecular mechanism of glutamatergic dysfunction, this body of work provided a rationale for using agents such as lithium and valproate that reduce excessive PKC activation to treat cognitive problems in prenatal cocaine-exposed individuals. In addition to dramatically alter dopaminergic and glutamatergic neurotransmission, prenatal cocaine exposure also have profound effects on neurotrophin signaling. Using brains from brains from 21-day-old rats that have had exposed to cocaine during gestation, we demonstrate an upregulated BDNF-TrkB signaling by enhancing BDNF binding affinity for TrkB. Since BDNF-TrkB regulates synaptic activity via interacting with NMDARs, these data together indicate the upregulated BDNF-TrkB may be a compensatory response to defects in glutamatergic signaling. I served as the primary investigator or co-investigator in all of these studies. I served as the primary investigator or co-investigator in all of these studies.

a. Wang HY, Runyan S, Yadin E, Friedman E (1995) Prenatal exposure to cocaine selectively affects D_1 dopamine receptor-mediated activation of striatal Gs proteins. J Pharmacol Exp Ther 273:492-498.
b. Jones LB, Stanwood GD, Reinoso BS, Washington RA, Wang HY**,** Friedman E, Levitt P (2000) In Utero cocaine-induced dysfunction of dopamine D_1 receptor signaling and abnormal differentiation of cerebral cortical neurons. J Neurosci 20: 4606-4614.
c. Bakshi K, Gennaro S, Chan CY, Kosciuk M, Liu J, Stucky A, Trenkner E, Friedman E, Nagele RG, Wang HY (2009) Prenatal cocaine reduces AMPA receptor synaptic expression through hyperphosphorylation of the synaptic anchoring protein GRIP. J Neurosci 29: 6308-6319.
d. Bakshi K, Parihar R, Goswami SK, Walsh M, Friedman E, Wang HY (2014) Prenatal cocaine exposure uncouples mGluR1 from Homer1 and Gq proteins. Plus One 9:e91671.
e. Stucky A, Bakshi K, Friedman E, Wang HY (2016) Prenatal cocaine exposure upregulates BDNF-TrkB signaling. Plos One 11 (8):e0160585.

3. To study functional changes in disease brains, I have adapted and fine-tuned functional studies that are typically used in cells and fresh tissues to analyze the signaling and protein-protein interaction in well-characterized diseased and well-matched control postmortem brains with short postmortem intervals. I call this experimental system the *ex vivo stimulation* paradigm. Using this investigation tool, I have identified changes in receptor-mediated signaling and enzymes such as PKC in bipolar brains. I also identified the α7 nicotinic receptor (α7nAChR) as a sub-pM high-affinity receptor for amyloid-β in AD brains. The interaction of amyloid-β with α7nAChR enables subsequent binding of multiple amyloid-β and internalization of the amyloid-β/α7nAChR complexes, accumulation of intracellular amyloid-β and plaque formation. Through binding to α7nAChR, amyloid-β activates several key kinases to promote tau

phosphorylation leading to neurofibrillary lesions and eventual appearance of neurofibrillary tangles. After my discovery that amyloid-β signals via the α7nAChR, many drug discovery programs aimed to disrupt the amyloid-β interaction with α7nAChR to reduce AD pathologies and cognitive impairments. One of such compound identified was S 24795 of Servier Laboratoires in France. Working with PTI, I later discovered that the amyloid-β toxic signaling that leads to neurofibrillary lesions and inflammation requires recruitment of filamin A. This novel finding led us to hypothesize that manipulating filamin A expression or conformation can reduce AD pathogenesis elicited by amyloid-β and thereby normalize synaptic activities and restores cognitive function. More recently, we are the first laboratory to illustrate Filamin A with distorted conformation is intimately involved in AD pathogenesis. This hypothesis was support by the identification of PTI-125 (currently in phase II clinical trial), a small molecule proprietary compound of PTI that binds aberrant filamin A with ultra-high affinity to restore filamin A naïve conformation and reduce AD plaques and neurofibrillary pathologies mouse models and importantly normalizes receptor and synaptic activities in both mouse and human postmortem brain tissues using *ex vivo stimulation* method. More recently, we are the first group to prove experimentally that insulin and IGF-1 receptor signaling defects are prevalently present in AD brains even without diabetes. Such findings indicate that treatment with antidiabetics such as incretin receptor agonists that reduce brain insulin resistance may be effective Alzheimer's disease therapeutics. These studies provide evidence that the *ex vivo stimulation* paradigm using postmortem AD brain tissues is an effective tool to discover broad-spectrum disease-modifying AD therapeutics. The above mentioned target-directed drug discovery programs are accompanied by research efforts on discovery of reliable AD specific diagnostic biomarkers. The effectiveness of AD treatments is closely related to early detection of the disease. These studies have led to identification of potential AD-specific biomarkers such as PTI-125 DX (currently in phase II clinical trial) in the body fluid and peripheral tissues obtained with non-invasive methods. I served as the primary investigator or co-investigator in all of these studies.

a. Wang HY**,** Lee DHS, D'Andrea MR, Peterson PA, Shank RP, Reitz AB (2000) β-Amyloid$_{1-42}$ binds to α7 nicotinic acetylcholine receptor with high affinity: implications for Alzheimer's disease pathology. J Biol Chem 275: 5626-5632.
b. Wang HY**,** Lee DHS, Davis CB, Shank RP (2000) Amyloid peptide Aβ$_{1-42}$ binds selectively and with picomolar affinity to α7 nicotinic acetylcholine receptors. J Neurochem 75: 1155-1161.
c. Wang HY, Li W, Benedetti N, Lee DHS (2003) α7 Nicotinic acetylcholine receptors mediate β-amyloid peptides-induced tau protein phosphorylation. J Biol Chem 278:31547-31553.
d. Wang HY, Stucky A, Liu J, Shen C, Trocme-Thibierge C, Morain P (2009) Dissociating β-amyloid from α7 nicotinic acetylcholine receptor by a novel therapeutic agent, S 24795 normalizes α7 nicotinic acetylcholine and NMDA receptor function in Alzheimer's disease brain. J Neurosci 29: 10961-10973.
e. Wang HY, Bakshi K, Frankfurt M, Stucky A, Goberdhan M, Shah SM, Burns LH (2012) Reducing Amyloid-related Alzheimer's disease pathogenesis by a small molecule targeting filamin A. J Neurosci 32(29): 9773-9784.
f. Talbot K, Wang HY, Kazi H, Han L-Y, Bakshi KP, Stucky A, Fuino RL, Kawaguchi KR, Samoyedny AJ, Wilson RS, Arvanitakis Z, Schneider JA, Wolf BA, Bennett DA, Trojanowski JQ, Arnold SE (2012) Brain insulin resistance demonstrated in Alzheimer's disease without diabetes is associated with dysregulated IRS-1 and implicated in impaired cognition. J Clin Inv 122(4): 1-23. (co-first author)
g. Wang HY, Lee K-C, Pei Z, Khan A, Bakshi K, Burns LH (2017) PTI-125 binds and reverses an altered conformation filamin A to reduce Alzheimer's disease pathogenesis. Neurobiol Aging 55: 99-114.
h. Wang HY, Trocmé-Thibierge C, Stucky A, Shah SM, Kvasic J, Khan A, Morain P, Quignot I, Bouguen E, Deschet K, Pueyo M, Mocaer E, Ousset P-J, Vellas B, Kiyasova V (2017) Increased Aβ42-α7 nicotinic acetylcholine receptor complex level in lymphocyte is associated with

apolipoprotein E4 driven Alzheimer's disease pathogenesis. Alzheimer's Research & Therapy 9:54 (DOI 10.1186/s13195-017-0280-8)

4. Using the *ex vivo stimulation* method, we directly demonstrated a defective NMDA receptor system in schizophrenia relevant to cognitive impairment. We subsequently identified the primary location of the defective NMDA receptor signaling as postsynaptic density and the molecular mechanism responsible for the NMDA receptor hypofunction as enhanced neuregulin- ErbB4 signaling and impaired Src tyrosine kinase. More recently, we identify defects in a metabotropic glutamatergic receptor system, mGluR5 that forms a positive reciprocal interaction loop with NMDARs can contribute to NMDAR hypofunction in schizophrenia. By providing the site and molecular mechanism of NMDA receptor hypofunction, this body of work improves our knowledge of pathogenesis of schizophrenia and enables development of novel therapeutic strategies. One such strategy is repetitive transcranial magnetic stimulation (rTMS) to improve NMDA receptor function and thereby alleviate cognitive impairment in schizophrenia. I served as the primary investigator or co-investigator in all of these studies. Since olfactory neuroepithelial cells derived from biopsy can be cultured and expanded for many generations without losing disease-specific phenotypes, we dedicate our efforts on developing these disease-specific changes into biomarkers for differential diagnosis and monitoring the effectiveness of therapeutic agents. These translational research projects are expected to facilitate novel diagnostic and therapeutic strategies into clinical practices in schizophrenia.

a. Hahn CG, Wang HY, Cho DS, Talbot K, Gur RE, Berrettini WH, Bakshi K, Kamins J, Borgmann-Winter K, Siegel SJ, Arnold SE (2006) Abnormally enhanced neuregulin 1-ErbB4 signaling contributes to NMDA receptor hypofunction in schizophrenia. Nature Medicine 12:824-828. (co-first author)
b. Hahn CG, MacDonald ML, Banerjee A, Cho DS, Kamins J, Nie Z, Borgmann-Winter KE, Grosser T, Pizarro A, Ciccimaro E, Arnold SE, Wang HY, Blair IA (2009) Post-synaptic Density Fractions Obtained from Human Postmortmem Brain Tissues. PloS One 4: e5251.
c. Wang HY, Crupi D, Liu J, Stucky A, Cruciata G, Di Rocco A, Friedman E, Quartarone A, Ghilardi MF (2011) rTMS enhances BDNF-TrkB signaling in both brain and lymphocytes. J Neurosci 31: 11044-11054.
d. Banerjee A, Wang HY, MacDonald ML, Borgmann-Winter KE, Stucky A, Kvasic J, Egbujo C, Talbot K, Hemby SE, Siegel SJ, Arnold SE, Gur RE, Hahn C-G (2014) Src hypoactivity is a convergent mechanism for NMDA receptor hypofunction in schizophrenia. Mol. Psychiatry doi:10.1038/mp.2014. 115. (co-first author)
e. Wang HY, MacDonald ML, Borgmann-Winter KE, Banerjee A, Sleiman P, Tom A, Khan A, Lee K-C, Roussos P, Siegel SJ, Hemby SE, Bilker WB, Gur RE, Hahn C-G. mGluR5 hypofunction is integral to glutamatergic dysregulation in schizophrenia. Mol Psychiatry (In press)
f. Borgmann-Winter K, **Wang HY**, Ray R, Willis BR, Moberg PJ, Rawson NE, Gur RE, Turetsky BI, Hahn CG (2015) Altered G protein coupling in olfactory neuroepithelial cells from patients with schizophrenia. Schizophr Bull doi:10.1093/schbul/sbv129.

RESEARCH GRANTS AND CONTRACTS

CURRENT FUNDED GRANTS AND CONTRACTS:

1. **Translating the function of *C. elegans* APL-1 into understanding the function of human APP.** 4/1/2020-1/31/2022

National Institute of Neurological Disorders and Stroke (Type: 1 R21 AG065890)
Co-PI (PI: Chris Li, Ph.D.) $135,000

2. mGluR5 hypoactivity is integral to glutamatergic dysregulation in schizophrenia.
12/1/2019-3/31/2024
National Institute of Mental Health (Type: 1 R01 MH116463-01)
Co-PI (PI: Chang-Gyu Hahn, MD, Ph.D.) $592,118

3. Treating Alzheimer's disease by reducing insulin resistance with incretin receptor agonists.
5/15/2018-2/28/2023
National Institute on Aging (Type: 1 R01 AG057658)
Co-PI (PI: Konrad Talbot, Ph.D.) $1,091,886

4. Development of PTI-125 DX, a blood-based diagnostic for Alzheimer's disease.
9/15/2017-6/30/2020
National Institute on Aging (Type: STTR 1R42AG057329)
Co-PI (PI: George B. Thorton, Ph.D.) $238,470
Phase I & II clinical trial on AD diagnostic marker

5. Linking peripheral and brain insulin resistance to AD neuropathology and cognition.
2018-2023
National Institute on Aging (Type: RF1AG059621)
Subcontract PI (PI: Zoe Arvanitakis, M.D., M.S) $864,903

6. Open-label extension of a 3-month blinded clinical trial for PTI-125.
08/01/2020-07/31/2022
National Institute on Aging (Type: STTR R44 AG 065152-01)
Subcontract PI (PI: Lindsay Burns, Ph.D.)

7. Multiple Ascending Dose clinical trial of PTI-125, a novel AD therapeutic candidate.
2018-2019
National Institute on Aging (Type: R44 AG 060878)
Subcontract PI (PI: Lindsay Burns, Ph.D.) $118,978
Phase II clinical trial on AD therapeutic candidate

8. Mechanism linking insulin resistance to brain structure, pathology and function.
2014-2019
National Institute of Neurological Disorders and Stroke (Type: R01NS084965)
Subcontract PI (PI: Zoe Arvanitakis, M.D., M.S.)
$300,000/yr

9. Lesion and Activity Dependent Corticospinal Tract Plasticity.
2013-2018
National Institute of Neurological Disorders and Stroke (Type: 2RO1-NS064004-06)
Investigator (PI: John Martin, Ph.D.) $300,000/yr

10. Influence of S 24795 on Aβ42-α7 high affinity interaction, Aβ42-induced tau phosphorylation, and intraneuronal accumulation of Aβ42 using rat brain slice organotypic cultures.

Institut De Recherches Internationales Servier 2005-2020
Principal investigator $10,000/yr

11. Evaluating the effects of NP-101 and other agents on blocking spreading depolarization.
Neuropharmalogic Inc. 2017-2018
$ 11,613

PAST FUNDED GRANTS AND CONTRACTS:

Development of a biomarker assay based on the interaction of filamin A with the α7 nicotinic acetylcholine receptor.
Pain Therapeutics Inc. 2012-2015
Principal investigator $124,822.15/yr

Exploring the anti-cancer potential of PTI's proprietary FLNA-binding compounds.
Pain Therapeutics Inc. 2012-2014
Principal investigator $30,000/yr

Profiling of Alzheimer's disease compounds on high affinity Aβ42 target using rat brain synaptosomes.
Institut De Recherches Internationales Servier 2012-2013
Principal investigator $173,189.96/yr

Pharmacological profiling of Alzheimer's disease compounds on Aβ42-induced tau phosphorylation using rat brain tissues.
Institut De Recherches Internationales Servier 2012-2013
Principal investigator $145,556.66/yr
(Amendment of $145,500 addition pending)

Research of proteinic markers in Alzheimer's disease.
Institut De Recherches Internationales Servier 2012-2013
Principal investigator $58,860/yr

Profiling of Servier compounds on Alzheimer's disease treatment potential using *in vitro* cell-free assays.
Institut De Recherches Internationales Servier 2011-2012
Principal investigator $58,087/yr (renew yearly)

Establishment of a medium throughput cell-free assay.
Institut De Recherches Internationales Servier 2011-2012
Principal investigator $100,000/yr
($10,000/year additional starting on 2013)

Neuronal responsiveness to lithium 2008-2013
National Institute of Mental Health (Type: RO1-MH080193)
Sub-contract collaborator (PI: Chang-Gyu Hahn, M.D., Ph.D.) $34,000/yr

Determination of enhanced basal coupling by receptors in spinal cord corresponding to Neuropathic injury and potential inverse agonists.
Pain Therapeutics Inc. 2005-2012
Principal investigator **$5,000/yr**

Proof of Concept Using Lead Compounds from Medicinal Chemistry. 2009-2012

Pain Therapeutics Inc.
Principal investigator $31,782/yr

Pharmacological profiling of Alzheimer's disease compounds on Aβ42-α7 high affinity interaction, Aβ42-induced tau phosphorylation, and Aβ42-mediated neuronal functions using rat brain slice organotypic cultures.
Institut De Recherches Internationales Servier 2007-2010
Principal investigator

Target identification of ultra-low-dose opioid antagonists in preventing the Mu opioid receptor – G protein coupling switch that occurs in opioid tolerance
Pain Therapeutics Inc. 2005-2010
Principal investigator

Neuregulin 1-erbB4 signaling in schizophrenia 2006-2010
National Institute of Mental Health (Type: RO1)
Sub-contract collaborator (PI: Chang-Gyu Hahn, M.D., Ph.D.)

Prenatal cocaine alters NMDA receptor assembly.
National Institute of Drug Abuse (Type:MIDARP) 2005-2010
Principal investigator (Program director: Eitan Friedman, Ph.D.)

Neuregulin 1- erbB4 – NMDAR signaling in Postmortem Brains
Stanley Foundation 2005-2008
Co-investigator (PI: Chang-Gyu Hahn, M.D., Ph.D.)

Prenatal Cocaine exposure induces AMPA receptor dysfunction.
CUNY Collaborative Incentive grant 2005-2007
Principal investigator

Underlying mechanism of the mu opioid receptor G-protein switch that occurs in opioid Tolerance and its prevention by ultra low dose opioid antagonists.
Pain Therapeutics Inc 2004-2006
Principal investigator

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Intracellular Beta-Amyloid Accumulation and Neuronal Degeneration in Alzheimer's Disease.
Alzheimer's Association. 2003-2006
Co-investigator P.I.: Robert G. Nagele, Ph.D.

Assessment of mu opioid receptor-G protein switching in oxycodone tolerance and neuropathic pain & it prevention by ultra-low-dose naltrexone.
National Institute of Mental Health/STTR 2004-2005
Principal investigator

Assessment of G-Portein coupling and signaling of the mu opioid receptor in morphine naïve And morphine tolerant rats using receptor stimulation by morphine vs morphine + naloxone.
Pain Therapeutics Inc. 2003-2004
Principal investigator

Destruction of the D_1 dopamine receptor and G protein coupling: 1998-2001

molecular mechanism of developmental abnormality induced by prenatal cocaine exposure.
March of Dimes Birth Defects Foundation,
Principal investigator

Age and vascular α1-adrenoceptor functional coupling. 1997-1999
National Institute of Aging,
Principal investigator

G proteins in desensitized vascular smooth muscle. 1995-1997
Alleghny-Singer Research Institute,
Principal investigator

Altered receptor-G protein coupling: 1995-1997
molecular mechanism of hypertension.
American Heart Association, Southeastern Pennsylvania Affiliate,
Principal investigator

Brain Structure and Function after Fetal Cocaine Exposure.
National Institute on Drug Abuse 1990-1994
Investigator PI: J. Harvey, Ph.D.

Neural, Endocrine, and Gastric Changes Induced by
Immobilization Stress. 1992-1993
Ciba-Geigy corperation,
Principal investigator

Alzheimer's Disease Related Alterations in Serotonin Receptors-
G Proteins Interation. 1992-1993
Alleghny-Singer Research Institute,
Principal investigator

Dopamine-linked phosphoinositide metabolism in brain. 1991-1995
National institute of Neurological disorders and Stroke 1996-2000
Investigator P.I. Eitan Friedman, Ph.D.

Effect of Age on Serotonin-Induced G Protein Activation. 1991-1992
Center for Gerontological Research,
Principal investigator

Protein kinase C in Mania and in Lithium's Actions. 1989-1994
National Institute of Mental Health
Co-investigator PI: E. Friedman, Ph.D.

Aging, Protein kinase C and Serotonin Release. 1988-1993
National Institute of Aging 1993-1998
Co-investigator PI: E. Friedman, Ph.D.

The Effect of Age on Human Protein kinase C. 1989-1990
American Federation for Aging Research (AFAR),

Principal investigator

Role of Protein Kinase C in Aging. 1988-1989
American Federation for Aging Research (AFAR),
Co-investigator PI: Jupiter Yeung, Ph.D.

Protein Kinase C in Alzheimer's Disease. 1988-1989
Alzheimer's Disease and Related Disorders Associations, Inc.(ADRDA)
Principal investigator

PENDING RESEARCH GRANTS AND CONTRACTS
Project Number: 1R01AG076124-01
PIs: Hussein Yassine, Hoau-Yan Wang, Zoe Arvanitaki
Title: **Brain cPLA2 as a mechanism for neuroinflammation in AD/ADRD with and without APOE4**

Project Number: R41 NS 108830
PI: Hoau-Yan Wang, Ph.D
Source: NIDDS
Title: **A natural product PP2A inhibitor for the treatment of migraine.**
The primary goal of this study is to determine whether blocking cortical spreading depolarization by a natural product
PP2A inhibitor can be therapeutically beneficial to treat migraine.
Dates of proposed project: 09/1/2018-02/28/2020
Annual Direct costs: $89,172

Project Number:
Co-PI: Hoau-Yan Wang, Ph.D **PI: Lindsay Burns, Ph.D.**
Source: NCI
Title: **PTI-910, a novel small molecule that suppresses mTOR and K-RAS by binding filamin A.**
The primary goal of this study is to determine the anti-cancer therapeutic efficacy of the PTI-910 in a preclinical setting.
Dates of proposed project: 04/1/2019-03/31/2020

Annual Direct costs: $48,059
Effort: 0.5 Academic
No budgetary and scientific overlap

PATENTS

1. Alzheimer’s disease assay in living patients
   US Patent No.: 11,385,221 (7/12/2022)
   Author: **Wang HY**, Burns Barbier LH
   An assay for Alzheimer's disease (AD) pathology in a living patient is disclosed wherein an amount of α7nAChR or TLR4 in a FLNA-captured protein complex or α7nAChR in an Aβ-captured protein complex or α7nAChR-FLNA, or TLR4-FLNA and/or α7nAChR-Aβ42 complex present as a protein-protein complex in a sample is compared to the amount in a standard sample from a person free of AD pathology. An amount greater than in the standard

sample indicates AD pathology. Also disclosed is an assay predictive of prognosis for treatment with a medicament in which the amount of an above protein or protein complex is compared to an amount in the presence of a medicament that binds to a FLNA pentapeptide and contains at least four pharmacophores of FIGS. 7-12. An amount of protein or protein complex determined in the presence of medicament that is less than the first amount indicates a favorable treatment prognosis.

2. Method for inhibiting growth of cancer cells

US Patent No: 10363239 (7/30/2019)

Author: Wang HY, Burns Barbier LH

This patent describes a method of inhibiting the growth of cancer cells is disclosed in which cancer cells that contain an enhanced amount relative to non-cancerous cells of one or more of phosphorylated mTOR, Akt1, ERK2 and serine2152-phosphorylated filamin A are contacted with an FLNA-binding effective amount of a compound or a pharmaceutically acceptable salt thereof that binds to the pentapeptide of filamin A (FLNA) of SEQ ID NO: 1 and exhibits at least about 60 percent of the FITC-labeled naloxone binding amount when present at a 10 ?M concentration and using unlabeled naloxone as the control inhibitor at the same concentration. A compound that binds to the FLNA pentapeptide preferably also contains at least four of the six pharmacophores of FIGS. 19-24.

3. Alzheimer’s disease assay in living patients

US Patent No.: 10,222,368 (3/5/2019)

Author: **Wang HY**, Burns Barbier LH

This patent describes an assay for Alzheimer's disease (AD) pathology in a living patient is disclosed wherein an amount of α7nAChR or TLR4 in a FLNA-captured protein complex or α7nAChR in an Aβ-captured protein complex or α7nAChR-FLNA, TLR4-FLNA and/or α7nAChR-Aβ42 complex present as a protein-protein complex in a sample is compared to the amount in a standard sample from a person free of AD pathology. An amount greater than in the standard sample indicates AD pathology. Also disclosed is an assay predictive of prognosis for treatment with a medicament in which the amount of an above protein or protein complex is compared to an amount in the presence of a medicament that binds to a FLNA pentapeptide and contains at least four pharmacophores.

4. Method for inhibiting tau phosphorylation

US Patent No.: 10,017,736 (7/10/2018)

Author: **Wang HY**, Burns Barbier LH

This patent describes a method of inhibiting phosphorylation of the tau protein and/or a TLR4-mediated immune response is disclosed. The method contemplates administering to cells in recognized need thereof such as cells of the central nervous system an effective amount of a of a compound or a pharmaceutically acceptable salt thereof that binds to a pentapeptide of filamin A (FLNA) of SEQ ID NO: 1, and contains at least four of the six pharmacophores of FIGS. 35-40.

5. Alzheimer’s disease assay in living patients

US Patent No.: 9,500,640 (11/22/2016)

Author: **Wang HY**, Burns Barbier LH

This patent describes an assay for Alzheimer's disease pathology in a living patient wherein the α7nAChR/FLNA, TLR4/FLNA and/or α7nAChR/Aβ42 complex levels as the predictive of prognosis for treatments.

6. Method for inhibiting growth of cancer cells
US Patent No.: 9,433,604 (9/26/2016)
Author: **Wang HY**, Burns Barbier LH
A method of inhibiting the growth of cancer cells is disclosed in which cancer cells that contain an enhanced amount relative to non-cancerous cells of one or more of phosphorylated mTOR, Akt1, ERK2 and serine2152-phosphorylated filamin A are contacted with an FLNA-binding effective amount of a compound or a pharmaceutically acceptable salt thereof that binds to the pentapeptide of filamin A (FLNA) of SEQ ID NO: 1 and exhibits at least about 60 percent of the FITC-labeled naloxone binding amount when present at a 10 ?M concentration and using unlabeled naloxone as the control inhibitor at the same concentration. A compound that binds to the FLNA pentapeptide preferably also contains at least four of the six pharmacophores of FIGS. 19-24.

7. Alzheimer's disease assay in living patients
US Patent No.: 9,354,223 (5/31/2016)
Author: **Wang HY**, Burns Barbier LH
This patent describes an assay for Alzheimer's disease pathology in a living patient wherein the α7nAChR/FLNA, TLR4/FLNA and/or α7nAChR/Aβ42 complex levels are greater than standard samples to indicate Alzheimer's disease.

8. Filamin A binding anti-inflammatory and analgesic.
US Patent No.: 9,340,558 (5/7/2016)
Author: Burns Barbier LH, **Wang HY**, Lin N-H, Blasko A.
This patent describes a novel class of powerful anti-inflammatory and/or mu opioid receptor agonistic analgesic agents that bind with high affinity to filamin A. Unlike the existing narcotics, these analgesic agents produce minimal tolerance and dependence.

9. Analgesia with minimal tolerance and dependence by a mu opioid receptor agonist that also binds filamin A.
US Patent No.: 8,722,851 (5/13/2014)
Author: **Wang HY**, Burns Barbier LH, Wang J.
This patent describes a novel class of analgesic agents that are agonists of the mu opioid receptor and bind with high affinity to filamin A. Unlike the existing narcotics, these analgesic agents produce minimal tolerance and dependence.

10. Filamin A binding anti-inflammatory and analgesic.
US Patent No.: 8,653,068 (2/18/2014)
Author: Burns Barbier LH, **Wang HY**, Lin N-H, Blasko A.
This patent describes another novel class of powerful anti-inflammatory and/or mu opioid receptor agonistic analgesic agents that bind with high affinity to filamin A. Unlike the existing narcotics, these analgesic agents produce minimal tolerance and dependence.

11. Filamin A binding anti-inflammatory and analgesic.
US Patent No.: 8,614,324 (12/24/2013)
Author: Burns Barbier LH, **Wang HY**, Lin N-H, Blasko A.
This patent describes another novel class of powerful anti-inflammatory and/or mu opioid receptor agonistic analgesic agents that bind with high affinity to filamin A. Unlike the existing narcotics, these analgesic agents produce minimal tolerance and dependence.

12. Filamin A binding anti-inflammatory and analgesic.
US Patent No.: 8,580,809 (11/12/2013)
Author: Burns Barbier LH, **Wang HY**, Lin N-H, Blasko A.
This patent describes another novel class of powerful anti-inflammatory and/or mu opioid receptor agonistic analgesic agents that bind with high affinity to filamin A. Unlike the existing narcotics, these analgesic agents produce minimal tolerance and dependence.

13. Filamin A binding anti-inflammatory and analgesic.
US Patent No.: 8,580,808 (11/12/2013)
Author: Burns Barbier LH, **Wang HY**, Lin N-H, Blasko A.
This patent describes another novel class of powerful anti-inflammatory and/or mu opioid receptor agonistic analgesic agents that bind with high affinity to filamin A. Unlike the existing narcotics, these analgesic agents produce minimal tolerance and dependence.

14. Analgesia with minimal tolerance and dependence by a mu opioid receptor agonist that also binds filamin A.
US Patent No.: 8,492,349 (7/23/2013)
Author: **Wang HY**, Burns Barbier LH, Wang J.
This patent describes a novel class of analgesic agents that are agonists of the mu opioid receptor and bind with high affinity to filamin A. Unlike the existing narcotics, these analgesic agents produce minimal tolerance and dependence.

15. Methode de criblage de composes aux proprietes anti-amyloide (Screening method of anti-amyloid compounds)
Patent No.: n°06/07385
Authors: **Wang HY**, Morain P, Thibierge C
This patent describes a novel method to select compounds that may retard β-amyloid induced neuronal dysfunction. The compounds identified through this screening program may be used to treat neurodegenerative diseases with amyloid pathologies including Alzheimer's disease and Down syndrome.

16. Method for treating neurodegenerative disorders
Patent No.: 7,018,797 (3/28/2006)
Authors: Reitz AB, Demeter DA, Lee DHS, **Wang HY**, Chen RH, Morgan Ross T, Scott MK, Plata-Salaman CR
This patent describes a novel method of treating a neurodegenerative disorder by inhibiting the interaction between Amyloid β and α7 nicotinic receptor.

17. Method of treating neurodegenerative disorders via inhibition of amyloid β binding.
Patent No.: 6,441,049

Authors: Reitz AB, Demeter DA, Lee DHS, **Wang HY**, Chen RH, Morgan Ross T, Scott MK, Plata-Salaman CR
This patent describes a novel method of treating a neurodegenerative disorder by inhibiting Amyloid β binding.

18. ErbB4 as a therapeutic target of psychotic illnesses
Penn T4328 application
Author: Hahn CG, **Wang HY**, Arnold S.
This patent describes a novel therapeutic approach to reduce psychotic episodes by reducing ErbB4 signaling.

INVITED PRESENTATION:

09/2019 VI International Workshop on Nitric Oxide in Cancer and Beyond
New York, USA
NMDA receptor-mediated signaling and activation of NOS in healthy human glia and glial tumors

04/2018 The 15th World Congress of the Society for Brain Mapping and Therapeutics
Los Angeles, USA
Reducing amyloid-related Alzheimer's disease pathogenesis by a small molecule targeting filamin A

09/2017 NYU Joint Fresco Institute & Neuroscience Research Meeting
New York, USA
Fluid biomarkers to tract Parkinson's disease progression

06/2015 NYC visiting fellowship in transcranial Magnetic Stimulation
New York, USA
Molecular effects of TMS in animals

07/2012 Alzheimer Association International Conference
Vancouver, Canada
PTI-125 reduces amyloid-related Alzheimer's pathogenesis by targeting filamin A.

03/2011 Institut De Recherches Internationales Servier
Croissy-Sur-Seine, France
Impaired Insulin Signaling in Hippocampal Formation of the Alzheimer's disease cases.

04/2010 The first international workshop on synaptic plasticity from bench to bed side.
Taomina, Italy
TMS-induced plasticity in an animal model: mechanisms of action

03/2010 Institut De Recherches Internationales Servier
Croissy-Sur-Seine, France
The Hunt for β-Amyloid - α7 Nicotinic Receptor Complex Breakers to Treat Alzheimer's disease.

06/2006 Workshop-"The Continuum between MCI and Alzheimer's Disease": From Physiopathology to Clinical and Regulatory Approaches.
Versailles, France
Nicotinic receptor and β-Amyloid

02/2005 Chemistry department, Stevens Institute of Technology
New Jersey, USA
A neuronal receptor for β-amyloid in our minds: Therapeutic implications for Alzheimer's disease treatments.

11/2004 Biology Colloquium, Biology department, City College of New York
New York, USA
A neuronal receptor for β-amyloid in our minds: Therapeutic implications for Alzheimer's disease treatments.

07/2004 Biomedical and pharmaceutical science center, China Medical University.
Taiwan
The role for β-amyloid in mediating Alzheimer's disease pathogenesis.

03/2002 Biochemistry seminar, Chemistry department, City College of New York
New York, USA
Pathway to neurodegeneration in Alzheimer's disease: The role of a neuronal receptor for β-amyloid.

07/2000 Graduate school of Pharmaceutical Sciences, China Medical University
Taiwan
Current development in pharmacotherapy for Alzheimer's disease.

09/1999 Johnson & Johnson annual research symposium
New Jersey, USA
α7 Nicotinic receptor as the target for Alzheimer's disease treatment.

CONSULTANCY AND SCIENTIFIC ADVISORY BOARDS:

1. **Institut De Recherches Internationales Servier** (Drug discovery, preclinical development)

2. **Cassava Sciences.** (Scientific advisory board member, drug discovery & Preclinical development)

3. **Neuropharmalogic, Inc.** (Scientific advisory board member, drug discovery & preclinical development)

PROFESSIONAL ORGANIZATIONS:

New York Academy of Science
Society for Neuroscience
American Society for Pharmacology and Experimental Therapeutics
Mid-Atlantic Pharmacology Society

Dept. of Molecular and Cell Biology, Harvard University, Affiliate member, CAP

JOURNAL REVIEWER:
J. Neurosci., J. Pharmacol. Exp. Ther., Eur. J. Pharmacol., J. Neurochem., Biol. Psychiatry, J. Gerontol. Bipolar disorder, Exp. Neurol., Pharmacol. Biochem. Behav. Brain Research, J Nuclear Med,

GRANT REVIEWER:
Israel Science Foundation
Bi-National Science Foundation
New Zealand Neurological Foundation
Alzheimer's Foundation
PSC-CUNY
New Jersey Cancer research commission
Israel Science Foundation

TEACHING AND MANGERIAL EXPERIENCE:
Lectured in Medical Pharmacology course to medical and graduate students.
Lectured in Medical Physiology course to medical students
Lectured in Molecular Cell Biology course to medical students
Course director of graduate course, Neuropharmacology of neuro-pyschological disorders.
Course director of Pharmacology course to Physician Assistant students.
Lectured in Neuroscience graduate course
Lectured in Pharmacology course (neuropharmacology) to nurse practitioners.
Supervising research projects of numerous graduate students and post-doctoral research fellows.
Serve as a thesis committee member for graduate students.

GRADUATE STUDENTS UNDER SUPERVISION:
Kalindi Bakshi
Andres Stucky
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Marissa Goberdhan
Amber Khan

COMMITTEE SERVICES:

Member of bio-safety committee	MCP-Hahnemann University	1996-1997
Member of Step 2 committee (Cell biology curriculum)	CUNY Medical School	2002
Member of Rudin Fellowship committee	CUNY Medical School	2004-
Member of Curriculum committee	CUNY Medical School	2005-2010
Member of Academic progress committee	CUNY Medical School	2010-
Member of Library Committee	CUNY Medical School	2010-
Member of Radiation safety committee	CCNY	2005-
Member of Molecular biology and Biochemistry Panel	CUNY	2007-
Member of Graduate center Faculty Review panel	CNUY Graduate Center	2015-

PUBLICATIONS:

Articles

1. Robinson S., Mogul AS, Taylor-Yeremeeva EM, Khan A, Tirabassi AD, **Wang HY** (2021) Stress diminishes BDNF-stimulated TrkB signaling, TrkB-NMDA receptor linkage and neuronal activity in the rat brain. Neuroscience 473:142-158.

2. Arvanitakis Z, Capuano, AW, **Wang HY**, Schneider JA, Bennett DA, Ahima RS, Arnold SE (2021) Brain insulin signaling and cerebrovascular disease in human postmortem brain. Acta Neuropathologica Comm 9:71.

3. Meade GM, Charron LS, Kilburn LW, Pei Z, **Wang HY**, Robinson S (2021) A model of negative emotional contagion between male-female rat dyads: effects of voluntary exercise on stress-induced behavior and BDNF-TrkB signaling. Physiol & Behav 234: 113286.

4. Arvanitakis Z, **Wang HY**, Capuano AW, Khan A, Taib B, Anokye-Danso F, Schneider JA, Bennett DA, Ahima RS, Arnold, SE (2020) Brain insulin signaling, Alzheimer's disease pathology, and cognitive function. Annals Neurology 88: 513-525.

5. Pei Z, Lee K-C, Khan A, Erisnor G, **Wang HY** (2020) Pathway analysis of glutamate-mediated, calcium-related signaling in glioma progression. Biochemical Pharmacology 176: 113814

6. **Wang HY**, Pei Z, Lee K-C, Lopez-Brignoni E, Nikolov B, Crowley CA, Marsman MR, Barbier R, Friedmann N, Burns LH (2020). PTI-125 Reduces Biomarkers of Alzheimer's Disease in Patients. J Prev Alzheimers Dis. 7: 256-264.

7. Pei, Z, Lee K-C, Khan A, **Wang HY** (2019) Hyper-activated insulin signaling cascade in human glioblastoma cells. Critical Rev Oncog 24: 243-250.

8. **Wang HY**, Capuano AW, Khan A, Pei Z, Lee K-C, Bennett DA, Ahima RS, Arnold SE, Arvanitakis Z (2019) Insulin and adipokine signaling and their cross-regulation in postmortem human brain. Neurobiol Aging 84: 119-130.

9. **Wang HY**, MacDonald ML, Borgmann-Winter KE, Banerjee A, Sleiman P, Tom A, Khan A, Lee K-C, Roussos P, Siegel SJ, Hemby SE, Bilker WB, Gur RE, Hahn C-G (2018). mGluR5 hypofunction is integral to glutamatergic dysregulation in schizophrenia. Mol Psychiatry doi: 10.1038/s41380-018-0234-y.

10. Arnold SE, Arvanitakis Z, Macauley-Rambach S, Koening A, **Wang HY**, Ahima R, Craft S, Gandy S, Buettner C, Stoeckel L, Holtzman D, and Nathan D (2018) Brain insulin resistance in type 2 diabetes and Alzheimer's disease: Concepts and conundrums. Nature Rev Neurol 14:168-181.

11. Burns LH and **Wang HY** (2017) Altered filamin A enables Aβ-induced tau hyperphosphorylation and neuroinflammation in Alzheimer's disease. Neuroimmunol Neuroinflammation 4:263-271.

12. Rajan TS, Ghilardi MF, **Wang HY**, Mazzon E, Bramanti P, Restivo D, Quartarone A (2017) Mechanism of action for rTMS: a working hypothesis based on animal studies. Frontiers in Physiol (doi: 10.3389/fphys.2017.00457)

13. **Wang HY**, Lee K-C, Pei Z, Khan A, Bakshi K, Burns LH (2017) PTI-125 binds and reverses an altered conformation filamin A to reduce Alzheimer's disease pathogenesis. Neurobiol Aging 55: 99-114.

14. Borgmann-Winter K, **Wang HY**, Ray R, Willis BR, Moberg PJ, Rawson NE, Gur RE, Turetsky BI, Hahn CG (2015) Altered G protein coupling in olfactory neuroepithelial cells from patients with schizophrenia. Schizophr Bull doi:10.1093/schbul/sbv129.

15. Fontanesi C, Kvint S, Frazzitta G, Bera R, Ferrazzoli D, Di Rocco A, Rebholz H, Friedman E, Pezzoli G, Quartarone A, **Wang HY**, Ghilardi MF (2015) Intensive rehabilitation enhances lymphocyte BDNF-TrkB signaling in patients with Parkinson's disease. Neurorehabilition & Neuronal Repair DOI: 10.1177/1545968315600272.

16. Banerjee A, **Wang HY**, MacDonald ML, Borgmann-Winter KE, Stucky A, Kvasic J, Egbujo C, Talbot K, Hemby SE, Siegel SJ, Arnold SE, Gur RE, Hahn C-G (2015) Src hypoactivity is a convergent mechanism for NMDA receptor hypofunction in schizophrenia. Mol. Psychiatry 20: 1091-1100 (doi:10.1038/mp.2014.115) ***Jointed first authors***

17. Talbot K, **Wang HY** (2014) The nature, significance, and GLP-1 analogue treatment of brain insulin resistance in Alzheimer's disease. Alzheimer's & Dementia 10: S12-S25. [review]

18. Yan H, Xu T, Lee K-C, **Wang HY**, Zhang Y (2013) Isoflurane increases neuronal cell death by downregulating miR-214. Plus One 8(2): e55276.

19. **Wang HY**, Bakshi K, Frankfurt M, Stucky A, Goberdhan M, Shah SM, Burns LH (2012) Reducing Amyloid-related Alzheimer's disease pathogenesis by a small molecule targeting filamin A. J Neurosci 32(29): 9773-9784.

20. Talbot K, **Wang HY**, Kazi H, Han L-Y, Bakshi KP, Stucky A, Fuino RL, Kawaguchi KR, Samoyedny AJ, Wilson RS, Arvanitakis Z, Schneider JA, Wolf BA, Bennett DA, Trojanowski JQ, Arnold SE (2012) Brain insulin resistance demonstrated in Alzheimer's disease without diabetes is associated with dyregulated IRS-1 and implicated in impaired cognition. J Clin Inv 122(4): 1-23. ***co-first authors***

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23. **Wang HY**, Stucky A, Hahn C-G, Wilson RS, Bennett DA, Arnold S (2011) BDNF-TrkB signaling in late life cognitive decline and Alzheimer's disease. Translational Neurosci 2: 91-100.

24. Burns LH and **Wang HY** (2010) Ultra-Low-Dose Naloxone or Naltrexone to Improve Opioid Analgesia: The History, the Mystery and a Novel Approach. Clinical Medicine Insights: Therapeutics 2: 857–868.

25. Burns LH and **Wang HY** (2010) PTI-609: A novel analgesic agent that binds filamin A to control opioid signaling. Recent Patents on CNS Drug Discovery 5: 210-220.

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36. Battaglia F, **Wang HY**, Gilardi MF, Gashi E, Quartarone A, Friedman E, Nixon RA (2007) Cortical plasticity in Alzheimer's disease in humans and rodents. Biol Psychiatry 62: 1405-1412. ***co-first authors***

37. Hahn CG, **Wang HY,** Cho DS, Talbot K, Gur RE, Berrettini WH, Bakshi K, Kamins J, Borgmann-Winter K, Siegel SJ, Arnold SE (2006) Abnormally enhanced neuregulin 1-ErbB4 signaling contributes to NMDA receptor hypofunction in schizophrenia. Nature Medicine 12:824-828. ***Jointed first authors***

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44. Nagele RG, D'Andrea MR, Lee H, Vekataraman V, **Wang HY** (2003) Astrocytes accumulate Aβ42 and give rise to astrocytic amyloid plaques in Alzheimer's disease brains. Brain Res 971:197-209.

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53. Seasholtz TM, Cai GP, **Wang HY,** Friedman E (2001) Ischemia-reperfusion decreases norepinephrine release and increases α-adrenoceptor-mediated contraction and inositol phosphate accumulation associated with increased coupling of α_{1a}-adrenoceptors to $G_{\alpha q}$ in the rat tail artery. J Appl Physiol 91: 1004-1010.

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63. **Wang HY,** Lee DHS, D'Andrea MR, Peterson PA, Shank RP, Reitz AB (2000) β-Amyloid$_{1-42}$ binds to α7 nicotinic acetylcholine receptor with high affinity: implications for Alzheimer's disease pathology. J Biol Chem 275: 5626-5632.

One of the 63 milestone papers in Alzheimer's disease research in year 2000 (selected from > 3000 published manuscripts by Alzheimer Forum).

64. **Wang HY**, Lee DHS, Wild KD, Shank RP (1999) Galanin inhibits acetylcholine release from rat cerebral cortex via a pertussis toxin-sensitive G_i protein. Neuropeptides 33: 197-205.

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